ROBUST SUMMARIES FOR
2,3-DIHYDRO-2,2-DIMETHYL-7-BENZOFURANOL

1. GENERAL INFORMATION

1.1. CAS NUMBER	1563-38-8
1.2. CHEMICAL NAME	2,3-dihydro-2,2-dimethyl-7-benzofuranol

2.0 PHYSICAL AND CHEMICAL DATA

2.1 MELTING POINT

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.5% purity
Method:	OECD 102
GLP:	Yes
Year:	2000
Results:	< 0 °C
Data Quality:	Code 1d
References:	FMC Corporation, Princeton, NJ

2.2 BOILING POINT

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.5% purity
Method:	OECD 103
GLP:	Yes
Year:	2000
Results:	76 °C @ 1 mm Hg, Vacuum distillation
Data Quality:	Code 1a
References:	FMC Corporation, Princeton, NJ

2.3 VAPOR PRESSURE

2.3.1 Extrapolated Value

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.5% purity
Method:	OECD 104
GLP:	Yes

Year:	2000
Results:	27.2 Pascals @ 20 °C, Static method. Extrapolated from higher temperature.
Data Quality:	Code 1a
References:	FMC Corporation, Princeton, NJ

2.3.2 Measured Value

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.56% purity
Method:	OECD 104/OPPTS 830.7950
GLP:	Yes
Year:	2003
Results:	1.14 Pa (8.55 x 10^{-3} mm Hg) at 25°C
Data Quality:	Code 1a
References:	Ambroz Hahn, J., "Vapor Pressure Determination of 7-Hydroxy Using the Gas Saturation Method", FMC Study Number: 000PCC02482, ABC Laboratories, Inc., Columbia, Missouri, 2003.

2.4 PARTITION COEFFICIENT

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.5% purity
Method:	OECD 107
Temperature:	23 °C
GLP:	Yes
Year:	2000
Results:	134, Flask-shaking method
Data Quality:	Code 1a
References:	FMC Corporation, Princeton, NJ

2.5 WATER SOLUBILITY

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol, 99.5% purity
Method:	OECD 105
Temperature:	25 °C
GLP:	Yes
Year:	2000

Results: 7.9 g/L

Data Quality: Code 1a

References: FMC Corporation, Princeton, NJ

3.0 ENVIRONMENTAL FATE AND PATHWAY

3.1 PHOTODEGRADATION

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol

Method: Following EPA Pesticide Assessment Guidelines, OPPTS 835.2210

Type: aqueous photodegradation

GLP: Yes

Year: 2000/ 2001

Light Source: Xenon arc lamp

Light Spectrum: 290-800 nm

Relative Intensity: Based on Intensity of Sunlight at 40 N latitude:

Spectrum of substance: Max lambda: 297.5

Max epsilon: 12

Remarks: The test medium was water. The test substance was exposed to simulated sunlight for an equivalent of 28 days with a 12 hour light/dark cycle and maintained at 25 C. Actinometer solutions of PNAP-PYR were used as well as dark controls. Triplicate samples were analyzed at specified timepoints.

Results: The half-life of 7-hydroxy when exposed to artificial sunlight at a concentration of 100 ppm in pH 7 buffer at 25 C was 9.9 days. See the following table for degradation at each timepoint. The quantum yield of 7-hydroxy was calculated using 40 N latitude during the summer season. The calculated quantum yield of 7-hydroxy (6.21×10^{-4} M) in pH 7 buffer was 3.25×10^{-1}.

Time (days)	Amount Remaining, Dark Control (%)	Amount Remaining, Light Exposed (%)
0	100	100
2	98	91
4	98	87
8	99	62
11	98	39
15	99	40

Remarks: The photolysis study is assigned a reliability code of 1a.

References: McKemie, T., "Photodegradation of 7-Phenol in Buffered Aqueous Solution at pH 7 Under Artificial Light," Unpublished study for FMC Corporation, Agricultural Products Group, Princeton, NJ, 2001.

3.2 STABILITY IN WATER (HYDROLYSIS)

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol

Method: OECD guideline 111

GLP: Yes

Year: 2000

Results: 7-hydroxy was tested at a concentration of 100 ppm at pH 4, 7 and 9 at 50 C for 5 days in the dark. Samples were analyzed by HPLC in triplicate at 0 and 5 days. The compound was stable at pH 4 and 7. For pH 9, the compound was further tested at 20 and 37 C for 35 days, sampling at 6 timepoints between 0 and 35 days. A concurrent test was run at pH 1.2 at 37 C with the same sampling points. See table below for results at pH 1.2 and 9.

pH	Temperature	Half-life
1.2	37 C	301 days
9	20 C	277 days
9	37 C	74 days

Remarks: The hydrolysis study is assigned a reliability code of 1a.

References: McKemie, T., "Hydrolysis of 7-Phenol at pH 4, 7 and 9," Unpublished study for FMC Corporation, Agricultural Products Group, Princeton, NJ, 2000.

3.3 TRANSPORT/DISTRIBUTION (FUGACITY MODEL)

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol

Method: Estimated by EPI Suite Program (v.3.11)

Inputs: Molecular weight: 164.21

Water solubility: 7900 mg/L

Vapor Pressure: 8.55E-03 mm Hg

Log Kow: 2.13

Boiling point: 76 C

Year: 2003

GLP: No

Results: Distribution using Level III Fugacity model

	Mass Amount	**Half-Life**	**Emissions**
	(percent)	(hr)	(kg/hr)
Air	0.26	3.43	1000
Water	37.5	900	1000
Soil	62.1	900	1000
Sediment	0.156	3.6e+003	0

Persistence Time: 591 hr

Remarks: The fugacity calculation by an acceptable method is assigned a reliability code of 2f.

References: Syracuse Research Corporation, Syracuse NY

Description of EPI-WIN Fugacity Model (Help File Excerpt):

EPIWIN v3 contains a Level III fugacity model. The methodology and programming approach was developed by Dr. Donald Mackay and co-workers (Mackay et al., 1996a, 1996b; Mackay 1991). The model in EPIWIN v3 is a direct adaptation of this methodology and approach. While it uses the same equations as Mackay's EQC Level III Fugacity Model, it was adapted specifically for use in EPIWIN. It uses exactly the same default values as the Mackay model (Note: an executable version of Mackay's EQC model can be downloaded from The Environmental Modeling Centre (Trent University) Internet web-site: http://www.trentu.ca/academic/aminss/envmodel/models.html).

A detailed description of Level I, II and III fugacity models is not presented here; please see the Mackay publications and Internet web-site cited above. In general, fugacity models predict the partitioning of an organic compound in an evaluative environment. A Level III model does not assume an equilibrium state; it only assumes steady-state. The Level III model in EPI predicts partitioning between air, soil, sediment and water using various user-input parameters and/or inputs estimated by several EPI programs.

Note: all Fugacity Half-Life Values, Emission Values, Soil Koc and Advection Values have default values or estimation methods. User intervention is not required to generate model predictions. However, more accurate user-input data (e.g. measured half-live data) should result in better model predictions. Also, modification of various default values may be required for individual evaluations. A discussion of each "Fugacity" menu selection follows.

Half-Life Values

Half-lives are required for air, soil, sediment and water ... the fugacity cannot run without them.

If the half-lives in air, water, soil and sediment are known, the "Use Half-Lives Entered Below" should be selected and the known values should be entered in the appropriate fields. Often, however, this data is not available and requires estimation. The BIOWIN and AOPWIN programs are used to make these estimates. The AOPWIN air estimate is based upon estimated hydroxyl radical and ozone rate constants. AOPWIN does have an experimental database containing more than 700 compounds. If an entered structure has a database match, the database value is used instead of the program estimate.

The water, soil and sediment half-lives are based upon BIOWIN prediction times for either ultimate or primary biodegradation. The prediction times range from "Hours" to "Recalcitrant". Each "time-range" has a default half-life value; these default values can be changed if desired. The

default values were derived by Dr. Robert S. Boethling of the U.S. EPA based upon the methodology reported in the Boethling et al. (1994) journal article. The default values in EPI v3.02+ are slightly different than the default values in prior versions of EPI. If BIOWIN predicts "Weeks" for biodegradation, then a half-life of 15 days is applied to water and soil ... a half-life of 60 days is applied to sediment because the default "Half-Life Factor" for sediment is 4 times the value for water and soil (again, the default "Half-Life Factors" were derived by Dr. Robert S. Boethling). Each Biowin half-life is multiplied by the "Half-Life Factors".

The Half-life entry box contains two buttons for "Set Biowin Half-life Values". The "EPA default" button sets the values derived by Dr. Robert S. Boethling. The "Alternative" button sets slightly more conservative values.

Emission Values

The default Environmental Emission Rates are 1000 kg/hr to Air, Water and Soil (Sediment has a value of zero); these are the Mackay defaults. The Air, Water and Soil rates can be modified if desired.

EPIWIN can run the level III model once per EPI run using the emission rates shown (this is the program default) or multiple times per EPI run. Currently, "Multiple Level III Output" will run the Level III model 7 times using all permutations of Air, Water and Soil rates as either 0 or 1000 (the permutation where all rates are 0 is excluded).

Advection Values

The Advection Times apply to Air, Water and Sediment. These values should not be changed unless you are very familiar with the Mackay model. Access is available for advanced use only.

Soil Koc Value

The Fugacity Model requires a soil Koc value. By default, the Mackay Model calculates the soil Koc from the log Kow value. If desired, the soil Koc can be estimated by the PCKOCWIN program or directly entered by the user.

Other Input Parameters

The Fugacity Model cannot run without a vapor pressure. If the vapor pressure is not user-entered, the model uses the vapor pressure estimate by the MPBPWIN Program. If the MPBPWIN Program estimates a vapor pressure of zero (which can occur if an estimate is less than 1.00e-40 mm Hg), the fugacity model uses an assumed value of 1.00e-15 mm Hg (this value is low enough to have no sensitivity effect in the fugacity estimates). See section 5.3 concerning Henry's law constant inputs. The model also requires a log Kow value. If the log Kow is not user-entered, the model uses the value from the KOWWIN Program (an experimental database value is used if available instead of the estimate).

The Fugacity model in EPIWIN has limited user-access to many parameters in the Mackay Level III Model. For example, parameters such as rain rate, aerosol deposition, soil water runoff, and diffusion mass transfer coefficients cannot be changed by the EPIWIN user. For these parameters, EPIWIN relies solely upon the defaults values as determined by Mackay and co-workers. This greatly simplifies application of a Level III model for most users. If you understand the inter-workings of a Level III model and need access to these parameters, you can download the Mackay EQC Model from the Internet web-site listed above.

3.4 BIODEGRADATION

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	OECD guideline 302B
Test type:	Zahn-Wellens/EMPA test
Inoculum:	fresh sewage treatment plant sample
Concentration of the chemical:	30 ppm

Contact time:	28 days
Degradation:	Degradation of the test substance was complete in 27 days.
GLP:	Yes
Year:	2002
Results:	The majority of the test substance (74.4%) had degraded by 1 day after treatment. The test substance was completely degraded by 27 days after treatment. Degradation of the reference substance (ethylene glycol) and 7-hydroxy occurred without any adaptation phase. Complete degradation of the reference compound within a 5-day period, no inhibitory effect of the test substance, and the decrease of dissolved organic carbon in the test suspension occurring gradually over a 27-day period showed the test was valid. Based on this data 7-hydroxy should not be expected to persist in the environment.
Remarks:	The biodegradation study is assigned a reliability code of 1a.
References:	McKemie, T., "Zahn-Wellens/EMPA Test for Biodegradation of 7-Phenol," Unpublished study for FMC Corporation, Agricultural Products Group, Princeton, NJ, 2002.

4.0 ECOTOXICOLOGY

4.1 ACUTE TOXICITY TO FISH

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol (99.4% purity)
Method:	U.S. EPA FIFRA 72-1 (c)
Species:	Rainbow trout, Oncorhynchus mykiss
Test Concentration (actual):	2.9, 7.0, 13, 21, 33, and 50 mg/L
Exposure Period:	96 hours
Analytical Monitoring:	Yes
GLP:	Yes
Year:	1998
Results:	96 hour LC50 = 37 mg/L NOEC = 7.0 mg/L The acute toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol ("7-hydroxy") to the rainbow trout, Oncorhynchus mykiss was conducted for 96 hours from August 20 to 24, 1998 at T.R. Laboratories, Inc., in Marblehead, Massachusetts. The test was performed under static conditions at 12 ± 1°C with 5 concentrations of test substance and a dilution water control (Total Organic Carbon <1.0 mg/L, Limit of Detection). The dilution water was deionized water collected at Marblehead, Massachusetts and adjusted to a hardness of 40 to 48 mg/L as

$CaCO_3$. Nominal concentrations of 7-hydroxy were 0 mg/L (control), 7.8 13, 22, 36 and 60 mg/L. Mean measured concentrations of 7-hydroxy were ND (none detected at or above the quantitation limit of 2.9 mg/L; control), 7.0, 13, 21, 33 and 50 mg/L. Mean measured concentrations were 83 to 100% of nominal values and were stable during the 96-hour test. Mean measured concentrations were used for all calculations.

Organisms used in the test were obtained from a commercial supplier and acclimated to test conditions for more that 14 days at the contract laboratory. Ten rainbow trout (juveniles) were indiscriminately distributed to each of two replicates of each treatment. The test was performed in 20-liter glass aquaria that contained 16 liters of test solution. Test vessels were randomly arranged in a water bath during the test. A 16-hour light and 8 hour dark photoperiod was automatically maintained with cool-white fluorescent lights that provided a light intensity of approximately 97 foot candles. After 96 hours of exposure, the control organisms had a mean wet weight (blotted dry) of 0.27 g and a mean total length of 31 mm. All animals were in good condition at the beginning of the study. Dissolved oxygen ranged from 7.7 to 9.7 mg/L during the study; pH ranged from 7.2 to 7.5, conductivity was 160 umhos/cm; temperature ranged from 11.5 to 12.6 ^{o}C, all measured for each group at 0, 24 48, 72 and 96 hours during the study.

Data Quality: Code 1

References: T.R. Wilbury Laboratories, Inc. Acute Toxicity of 7-Hydroxy to the Rainbow trout, Oncorhynchus mykiss. T.R. Wilbury Study Number 1583-FM. FMC Study Number A98-4812. (1998)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol (99.4% purity).

Method: U.S.EPA FIFRA 72-2

Species: Daphnia magna

Exposure Period: 48 hours

Analytical Monitoring: Yes

GLP: Yes

Year: 1998

Results: LC50 = 40 mg/L

EC50 = 33 mg/L

NOEC = 13 mg/L

The acute toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol (" 7-hydroxy") to the daphnid, Daphnia magna, was conducted for FMC Corporation for 48 hours from September 1 to 3, 1998 at T.R. Wilbury Laboratories, Inc., in Marblehead, Massachusetts.

The test was performed under static conditions at 20 ± 1°C with five concentrations of test substance and a dilution water control. The dilution water was deionized water collected at Marblehead, Massachusetts and adjusted to a hardness of 160 to 180 mg/L as $CaCO_3$ (Total Organic Carbon of <1.0 mg/L, Limit of

Detection). Nominal concentrations of 7-hydroxy were 0 mg/L (control), 13, 22, 36, 59, and 100 mg/L. Mean measured concentrations of 7-hydroxy were ND (none detected at or above the quantitation of 2.9 mg/L; control), 13, 21, 35, 57 and 97 mg/L that were 95 to 100% of nominal and were stable throughout the test. . Dissolved oxygen ranged from 8.1 to 8.4 mg/L during the study; pH ranged from 7.4 to 7.6, conductivity was 560-570 umhos/cm; temperature ranged from 19.0 to 19.6 ^{o}C, all measured for each group at 0, 24 and 48 hours during the study.

Organisms used the test were obtained from an in-house culture that was acclimated to test conditions for more than seven days at the contract laboratory. Ten daphnids were indiscriminately distributed to each of two replicates of each treatment. The test was performed in 300 ml glass beakers that contained 250 ml of test solution. A 16 hour light and 8 hour dark photoperiod was automatically maintained with cool-white fluorescent lights that provide a light intensity of approximately 50 foot candles. After 48 hours of exposure the control organisms had an average wet weight (blotted dry) of 0.14 mg. All animals were in good condition at the beginning of the study. One hundred percent survival occurred in the control and no sub lethal effects were noted in the control during the exposure period.

Data Quality: Code 1

References: T.R Wilbury Laboratories, Inc. Acute Toxicity of 7-Hydroxy to the Daphnid, Daphnia magna. T.R. Wilbury Study Number 1584-FM. FMC Study Number A98-4811. (1998)

4.3 TOXICITY TO AQUATIC PLANTS

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol (99.4% purity)

Method: U.S. EPA FIFRA Subdivision J, 123-2

Species: Selenastrum capricornutum

Exposure Period: 120 hour

GLP: Yes

Year: 1998

Results: Areas under the Growth Curve

Dose Group	72 hours	96 hours	120 hours
0 (Control)	853,000	4,207,000	7,567,000
6.2 mg/L	803,000	4,707,000	9,447,000
13 mg/L	737,000	3,660,000	9,087,000
25 mg/L	507,000	3,273,000	7,593,000
50 mg/L	459,000	2,367,000	6,620,000
99 mg/L	185,000	573,000	2,213,000

Endpoint	Calculated Using Cell ensity	Calculated Using Average Specific Growth Rate	Calculated Using Area under the Growth Curve
72 hour EC50	44 mg/L	>99 mg/L	44 mg/L
96 hour EC50	50 mg/L	>99 mg/L	50 mg/L
120 hour EC50	72 mg/L	>99 mg/L	94 mg/L
NOEC	50 mg/L	50 mg/L	

Remarks:

The toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol ("7-hydroxy") to the freshwater alga, Selenastrum capricornutum, was investigated. The test, which was designed to establish the 24, 48, 72, 96 and 120 hour EC25 and EC50 values and the 120 hour no observed effect concentration (NOEC), was conducted from August 28 to September 2, 1998 for FMC Corporation by T.R. Wilbury Laboratories, Inc.

The test was conducted under static conditions with five concentrations of test substance and a dilution water control at 25 ± 2°C. The test substance was weighed and brought up to volume with algal media. Solutions wer prepared fresh for the stud on day 0. The dilution water was sterile enriched medium, containing 0.30 mg/L sodium EDTA, adjusted to a pH of 7.5 ± 0.2 with hydrochloric acid (10 mg/L particulate matter, <1.0 mg/L Total Organic Carbon, Limit of Detection). The number of cells/mL was determined microscopically using a haemocytometer every 24 hours during the exposure. Nominal concentrations of 7-hydroxy were 0 mg/L (control, 6.4, 13, 26 52 and 100 mg/L. Mean measured concentrations were <2.9 mg/L 9control), 6.2, 13, 25, 50 and 99 mg/L, which were 96% to 100% of nominal concentrations and were stable throughout the test. Mean measured concentrations were used for all calculations.

Algae were distributed among four replicates of each treatment at the rate of approximately 3000 cells/mL. The fourth replicate was established for the purpose of obtaining a 72 hour pH measurement (pH in this replicate was also recorded at 120 hours). Test vessels were 250 mL glass Erlenmeyer flasks that contained 50 mL of test solution with an approximate depth of 1.5 cm. Test vessels were randomly arranged on a rotary shaker that was adjusted to 100 rpm and located in an incubator during the test. A 24 hour light 0 hour dark photoperiod was automatically maintained with cool-white fluorescent lights that provided a light intensity of 4,000 to 4,400 lux.

No insoluble material was observed during the test.

Data Quality:

Code 1

References:

T.R. Wilbury Laboratories, Inc. Growth and Reproduction Toxicity Test with 7-Hydroxy and the Freshwater Alga, Selenastrum capricornutum. T.R. Wilbury Study Number 1585-FM. FMC Study Number A98-4813. (1998)

5.0 TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ORAL

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	An oral LD50 was conducted with test material administered undiluted by gavage in accordance with EPA Guideline 81-1. Groups of animals (10/sex/group) were administered a single treatment via gavage to various doses of test material. Observations for toxicity and mortality were conducted at 0.5, 1, 2, 3, 4 and 6 hours on the day of dosing and twice daily for 13 days. On day 14 the animals were observed once. Body weights were recorded on days 0, 7 and 14 of study.
Species/strain:	Sprague-Dawley rats
Sex:	Both
No. Animals/Group:	10/sex/group
Post dosing observation period:	14 days
GLP:	Yes
Year:	1984
Results:	Oral LD50 in males is 2450 mg/kg (2137-2764, 95% confidence limits) and oral LD50 in females is 1743 mg/kg (1362-2124 mg/kg, 95% confidence limits). Practically non-toxic orally. Doses of 3000, 2300 and 1800 mg/kg were run in males with mortality of 80%, 40% and 10%, respectively, and doses of 2300, 1800, 1400 and 1000 mg/kg were run in females with mortality of 70%, 50%, 40% and 10%, respectively. Clinical signs noted included the following: prostration, recumbency, tremors, decreased locomotion and nasal, ocular and oral discharges. All signs of toxicity subsided by day two of the study. There were no target organ effects noted.
Data Quality:	Code 1
References:	Acute Oral Toxicity of FMC 10272 in Rats. FMC Toxicology Laboratory, FMC Study A83-1133, March 12, 1984. U.S. Environmental Protection Agency Pesticide Assessment Guidelines; Subdivision F, Hazard Evaluation: Human and Domestic Animals, 81-1 Acute Oral Toxicity Study.

5.1.2 DERMAL

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	Preliminary dermal toxicity and irritation screen. Groups of five male rabbits were exposed to test material in contact with intact skin for 24 hours under an occlusive wrap. Observations for toxicity and mortality were made every three hours on the day of dosing and once/day thereafter for 14 days. Skin irritation was scored using the Draize method at 24, 48, and 72 hours after application and on days 4, 7, and 14 of study.
Species/strain:	New Zealand White rabbits

No. Animals:	5 males/dose
Dose:	20 mg/kg and 300 mg/kg
Vehicle:	Undiluted
Exposure Period:	24 hours
Post-exposure observations:	14 days
GLP:	Yes
Year:	1985
Results:	Non-irritating at 20 mg/kg and minimally irritating at 300 mg/kg. No irritation was observed on rabbits receiving 20 mg/kg until day 7. Two rabbits had slight erythema. All irritation resolved by day 14. Rabbits treated with 300 mg/kg had no irritation at 24 and 48 hours. At the 72-hour scoring and on day 4, one rabbit had slight erythema. On day 7 one rabbit had eschar and one rabbit had slight erythema and desquamation. A third rabbit had desquamation. Dermal LD50 is greater than 300 mg/kg (no deaths occurred in the study). Practically non-toxic dermally.
Data Quality:	Code 2
References:	Preliminary Dermal Toxicity/Irritation of FMC 10272 Technical in Rabbits, FMC Toxicology Laboratory, FMC Study A84-1534, July 3, 1985.

5.1.3 INHALATION

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	Animals (5/sex/group) were exposed in a dynamically-operated whole-body inhalation chamber for six hours to a nominal vapor concentration of 0.03 mg/L or 4.5 ppm test material (measured with a Bendix THC Analyzer). The test atmosphere was generated by passing air over a reservoir of test material. Observations for mortality and toxicity were performed frequently during exposure and twice daily for 13 days and once on day 14. Body weights were recorded individually on day 0, 7 and 14. A control group of rats was sham-exposed to room air only.
Species/strain:	Sprague-Dawley rats
No. Animals:	5 male and 5 females
Dose:	0.03 mg/L or 4.5 ppm (nominal) or 18 ppm (analytical)
Vehicle:	undiluted
Exposure Period:	6 hours
Post-exposure observations:	14 days
GLP:	Yes
Year:	1987

Results:	There were no deaths or changes in body weight due to treatment during the study. The only clinical sign noted was red periocular fur in one male upon removal from the chamber and at the one-hour post-exposure observation. All other animals remained healthy during the study. The 6 hour LC50> 18 ppm, the maximum attainable concentration and a saturated vapor concentration
Data Quality:	Code 1
References:	Acute Inhalation Toxicity Screen of FMC 10272 in Rats, FMC Toxicology Laboratory, FMC Study A85-1662, March 24, 1987.

5.2 GENETIC TOXICITY IN VITRO

5.2.1 IN VITRO

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	L5178Y TK+/- Mouse Lymphoma Mutagenicity Assay. Duplicate assays were performed. L5178Y cells were grown in culture. Cell suspensions containing one million cells per ml. Test material was prepared in DMSO and diluted to concentrations ranging from 0.001 to 100 ul/ml. Test material, cell suspension, S9 mixture or culture media (non-activated assay) were added to each tube. Tubes were gassed with air and 5% carbon dioxide for four hours. After the four-hour exposure period, the cells were centrifuged, washed twice and evaluated for toxicity be comparing cell population growth at each dose level to that of solvent control cultures. For the mutation assay, appropriate concentrations of test article with or without S9 were added to cell suspensions to give final cell concentrations of 600,000 cells/ml. Solvent controls were used as negative controls. Positive control cultures included the edition of Ethyl Methanesulfonate (1.0 and 0.5 ul/ml) and 7, 12-Dimethylbenz(a)anthracene (7.5 and 5.0 ug/ml). All tubes were gassed and incubated for four hours at 37 degrees Centigrade under amber lighting. Following exposure, the cells were washed and removed by centrifuge and incubated for two days with cell population adjusted daily to 300,000 cells/ml. Following this expression period, cells were placed in cloning medium with 0.34% Noble agar and TFT (3 ug/ml final concentration) as a restrictive agent. For each pair of duplicate culture flasks one was used for viable count and one for labeling with TFT. Three plates each for the viable count and the labeling of cultures were incubated in petri plates. Petri plates were placed in cold storage for 20 minutes to allow gelling, the removed and incubated at 37 degrees Centigrade for 10-12 days. After the incubation period, the plates were scored for total number of colonies per plate. Mutation frequency was determined by dividing the average number of colonies in the three TFT plates by the average number of colonies in the three corresponding viability count plates and multiplying by two.
System of Testing:	Cultured L5178Y mouse lymphoma cells
Concentrations:	S-9 activated test cultures were dosed at 0.010, 0.0075, 0.0056, 0.0042, 0.0032, 0.0024, 0.0018 and 0.0013 ul/ml. Non-activated test cultures were dosed at 0.24, 0.18, 0.13, 0.10, 0.075, 0.056, 0.042, 0.032, 0.024 and 0.018 ul/ml.
Metabolic Activation:	Yes, S-9 rat liver microsomes
GLP:	No, but there were quality assurance audits

Year:	1983
Results:	Positive in the presence and absence of metabolic activation by S-9. Non-activated cultures cloned (top four doses) exhibited mean mutant frequencies of from 4.1 to 3.0 times the solvent control mutant frequencies. Total Growth for these cultures ranged from 6% to 25%. None of the other, lower doses in the non-activated assay had elevated mutant frequencies relative to the solvent control. The total growth of these doses ranged from 54-125%. Two activated cultures that were cloned (0.010 and 0.0075 ul/ml doses) exhibited mutant frequencies where were 3.3 and 2.1 times the mutant frequency of the solvent controls, respectively. The Total Growth of these cultures was 20% and 16%, respectively. None of the lower doses in the activated assay exhibited elevated mutant frequencies relative to the solvent controls. The total growth of these doses ranged from 44-100%. Appropriate positive and negative controls were included and showed the appropriate responses.
Data Quality:	Code 2
References:	L5178Y TK+/- Mouse Lymphoma Mutagenesis Assay, Microbiological Associates, FMC Study A83-961, September 13, 1983. Clive, D. and Spector, J.F.S. Laboratory procedure for assessing specific locus mutations at the TK locus in cultured L5178Y Mouse Lymphoma cells. Mutation Research 31, 17-29 (1975).

5.2.2 IN VITRO

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol
Method:	*Salmonella typhimurium*/Mammalian Microsome Plate Incorporation Assay (Ames Test). Nine separate, GLP studies with nice separate lots of the test material were conducted using *Salmonella typhimurium* tester strains TA1535, TA1537, TA1538, TA98, TA100 with and without metabolic activation by rat liver microsomes, S9, using the standard protocol. Appropriate positive and negative controls were included in all assays.
Type:	In vitro mutagenicity in bacteria
System of Testing:	*Salmonella typhimurium* TA1535, TA1537, TA1538, TA98, TA100 with and without metabolic activation by rat liver microsomes, S9
Concentration:	61 to 10,000 ug/plate
Metabolic Activation:	S9
GLP:	Yes
Year:	1983-1984
Results:	Positive: The same result was confirmed in all of the nine assays. The test material did not induce an increase in mutant frequency in tester strains TA1537, TA1538, TA98, or TA100 in the presence or in the absence of metabolic activation. The test material did induce a statistically significant positive or weakly positive response in tester strain TA1535 without metabolic activation at nontoxic doses (61-556 ug/plate; 123-3333 ug/plate). Mutant frequency was approximately 2.5 – 3.0 times the solvent control in TA1535

without metabolic activation. Appropriate positive and negative controls were included in each assay and responded appropriately.

Data Quality: Code 1

References:

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-842, Hazleton Laboratories America, Inc., March 19, 1984

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-843, Hazleton Laboratories America, Inc., May 9, 1984.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-911, Hazleton Laboratories America, Inc., December 5, 1983.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-927, Microbiological Associates, October 13, 1983.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-928, Microbiological Associates, September 28, 1983

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-930, Microbiological Associates, September 28, 1983.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-936, Microbiological Associates, September 28, 1983.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-937, Microbiological Associates, September 22, 1983.

Salmonella typhimurium/Mammalian Microsome Plate Incorporation Assay, FMC Study A83-942, Microbiological Associates, April 12, 1984-check date

Ames, B.N. McCann, M. and Yamasaki, E. Methods for Detecting Carcinogens and Mutagens with the *Salmonella* Mammalian-Microsome Mutagenicity Test, Mutation Res. 31, 347-364, 1975.

5.3 GENETIC TOXICITY IN VIVO

5.3.1 IN VIVO

Test Substance: 2,3-dihydro-2,2-dimethyl-7-benzofuranol

Method: Drosophila sex-linked recessive lethal assay: Adult males (8 to 30 hours old and previously starved for 4 hours) were treated in groups of 15 in vials plugged with cotton. The base of each vial was covered with a disc of filter material impregnated with 450 ul of sucrose feeding solution, with or without test material. Untreated controls received the untreated sucrose feed stock. The male flies were transferred to fresh treatment vials daily for 3 days. At the end of each 24-hour exposure period, the number of dead flies were counted. A positive control group was treated with 25 ppm dimethylnitrosamine for 24 hours. Following the exposure period, males were mated at age 3-4 days. Treated and control P1 Canton S wild-type males were mated singly to 3 virgin Baac females (age 3 to 10 days). Each male was transferred after 3 days to 3 new virgin females. The fertilized females of brood 1 were kept in culture vials for 4 more days the

	discarded. This transfer process was repeated twice more, but the time that the males in broods 2 and 3 was two days each. The males were then discarded. The F1 females (heterozygous for the treated X and the balancer X) were mated individually to brothers. An effort was made to mate 33 females from each P1 male brood to insure that a total of 99 chromosomes were tested from each treated male. Due to post-mating mortality and sterility, this number was sometimes less than 99 per male. The F2 generation cultures were observed when fully hatched for the presence (non-lethal) or absence (lethal) of wild type males. Suspected lethal cases were retested by re-mating with heterozygous females and observing the F3 offspring.
Species/strain:	Drosophila melanogaster
Sex:	Baac females and Canton-S wild-type males
Route of Administration:	Via feeding in 5% buffered sucrose solution
Exposure Period:	Three days
Doses:	A range-finding study was conducted to determine doses for the definitive study. Doses of 200, 250, 300, 350, 400, 450, 500 and 1000 ppm were employed in the definitive study.
Vehicle:	A stock solution was prepared by mixing 60 ul of test material to 4950 ul of 95% ethanol. Aliquots of the stock solution were mixed with the sucrose feeding solution to prepare a series of concentrations of test material in 10% ethanol. The negative control group was fed 5% buffered sucrose in 10% ethanol.
GLP:	Yes
Year:	1983
Results:	Negative. Test material does not induce sex-linked recessive lethal mutations *in vivo* in Drosophila.
Data Quality:	Code 2
References:	Drosophila Sex-Linked Recessive Lethal Assay of 2, 2-dimethyl-2,3-dihydro-7-hydroxybenzofuran ("7-hydroxy", T2049), University of Wisconsin, Zoology Department and Microbiological Associates, FMC Study A83-1020, November 7, 1983. Margolin, B.H., Collings, B. J. and Mason, J. M. Statistical analysis and sample size determinations for mutagenicity experiments with binomial responses. Environ. Mut. 5, 705-716 (1983).

5.3.2 IN VIVO

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol (99.5% purity)
	Method: The micronucleus assay was performed in two phases. The first phase, designed to set dose levels for the definitive study, consisted of a pilot toxicity study followed by a toxicity study. The second phase was the micronucleus assay study. In both phases, the test and control articles were administered in a constant volume of 20 mL/kg body weight by a single intraperitoneal injection. Corn oil was the solvent of choice; the test article was soluble in corn oil at 100 mg/mL, the maximum concentration tested in the study.

Guideline:	OECD 474
Type:	Micronucleus assay
Species/strain:	ICR mouse
Sex:	Male
Route of Administration:	Intraperitoneal
	Exposure Period: Single application
	Doses: 25, 50, 100 mg
GLP: (Yes or No)	Yes
Year:	2001
Results:	In the pilot toxicity study, male mice were dosed with 1, 10, 100 or 1000 mg test article/kg body weight and male and female mice were dosed with 2000 mg/kg. Mortality was observed in 2/2 male mice at 1000 mg/kg and in 5/5 male mice and 5/5 female mice at 2000 mg/kg. Clinical signs included lethargy in males at 10 and 100 mg/kg and piloerection in male mice at 100 mg/kg. In the toxicity assay, male and female mice were dosed with 200, 400, 600 or 800 mg test article/kg body weight. Mortality was observed in 2/5 male mice and 1/5 female mouse at 200 mg/kg, in 4/5 males and 2/5 females at 400 mg/kg and in 5/5 males and 5/5 females at 600 and 800 mg/kg. Clinical signs included lethary, piloerection, crusty eyes and hunched position in males and females at 200 and 400 mg/kg. In addition, convulsions were noted immediately after dose administration in males and females at 400, 600 and 800 mg/kg. Due to no differences in test article toxicity between males and females, the micronucleus assay was conducted using only male mice. In the micronucleus assay, male mice were dosed with 25, 50 or 100 mg test article/kg body weight. No mortality was observed in any male or female mice in the micronucleus study. Clinical signs included lethargy and piloerection in males and females at 50 and 100 mg/kg. All other mice treated with the test or control articles appeared normal following dose administration. Bone marrow cells, collected 24 and 48 hours after treatment, were examined microscopically for micronucleated polychromatic erythrocytes. A slight reduction of 4% in the ratio of polychromatic erythrocytes to total erythrocytes was observed in the group treated with 50 mg/kg relative to the respective vehicle control. This reduction suggests that the test article did not inhibit erythropoiesis. No significant increase in micronucleated polychromatic erythrocytes in test article-treated groups relative to the respective vehicle control groups was observed in male mice at 24 or 48 hours after dose administration ($p>0.05$). The results indicate that the test article did not induce a significant increase in micronucleated polychromatic erythrocytes in male mice. The test article was negative in the mouse micronucleus assay.
Data Quality:	Code 1a
References:	Gudi, R. and Krsmanovic, L. “Mammalian erythrocyte micronucleus test”, BioReliance, FMC Study A2000-5265, unpublished.

5.4 COMBINED REPEATED DOSE WITH REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol (99.5% purity)
Species/strain:	Wistar rats
No. Animals:	Eight groups – Main groups: 20 rats (10 male and 10 female) Recovery groups: 10 rats (5 male and 5 female); Control recovery and high dose recovery
Sex:	Male and female
Dose:	0, 100, 1000, 5000, 10000, 20000 ppm
Route of Administration:	Diet
Control group:	Yes
Exposure Period:	54 days
Frequency of Treatment:	Daily
Method:	7-hydroxybenzofuran was tested in Wistar rats in a combined repeated dose toxicity study with reproduction/developmental toxicity screening test. The test material was mixed with experimental food at concentrations of 100, 1000, 5000, 10000 and 20000 ppm. A concurrent control group and control recovery group received acetone mixed food. There were 10 male and 10 female rats per group and the recovery groups consisted of 6 male and 6 female rats per group. The prepared experimental group was fed prior to the mating period, during mating period and during post-mating period (in males), during pregnancy and up to lactation day 4 (in females). In the control recovery and high dose (recovery) groups the treatment period was followed by a 14-day no-treatment (recovery) period. The recovery period of the study started from the day of sacrifice of the first littered animals. The prepared experimental food was determined analytically for active ingredient at two separate times (day-0 of treatment and at 2nd month of the treatment period). The stability and homogeneity of the test item in the experimental food was confirmed prior to the start of the treatment and experimental food preparation was done within the stability period. Animals from all the groups were observed for clinical signs, physical abnormalities, changes in body weight, food consumption and survival. The functional observation battery was done shortly before sacrifice for 5 male and 5 females randomly selected from each group. For recovery groups functional observation was conducted along with the main groups. Hematology and clinical chemistry were performed for 5 males and 5 females randomly selected from each group at the end of the pre-mating period and recovery period. Histopathological examination of all the tissues from the randomly selected 5 males and 5 females from control and high dose groups were carried out. The data were statistically analyzed.
GLP: (Yes or No)	Yes
Guideline:	OECD 422

Year:	2002
Results:	Concentrations of 100, 1000 and 5000 ppm did not have any adverse effects on general health, body weight, food consumption, functional observation battery, hematological and biochemical parameters and reproductive performance of dams and sires. At 10,000 ppm, no treatment-related effects were seen on general health, body weights, functional observation battery, hematological and biochemical parameters. Food consumption, gestation body weight and litter size were decreased. At 20,000 ppm, body weight, food consumption, maternal body weight and food consumption during gestation and lactation period, litter size, mean viable litter size, mean number of corpora lutea, mean number of implantations and terminal fasting body weights were decreased. Liver weight ratios increased. Under the conditions of the study, the No Observed Adverse Effect Level (NOAEL) was determined to be 5000 ppm that is equivalent to 296.5 and 448.3 mg/kg/bw/day for males and females, respectively.
Data Quality:	Code 1a
References:	Krishnappa, H. "Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test with 7-hydroxybenzofuran in wistar rats", Rallis Research Centre, FMC Study A2000-5242, May 18, 2002, unpublished.

5.5 DEVELOPMENTAL TOXICITY/TERATOGENECITY

Test Substance:	2,3-dihydro-2,2-dimethyl-7-benzofuranol (purity of 99%)
METHOD:	Sprague-Dawley CD pregnant rats (8/group) received 0, 100, 500 or 1000 mg/kg/day of undiluted test material on gestation days 6-19 in a pilot teratology study. The age of the animals was young adult. Clinical signs were recorded daily; body weights and food consumption were recorded for days 0 and 6 and at three-day intervals during treatment. On gestation day 20, dams were euthanized and underwent Cesarean sectioning; each dam was examined for the number and distribution of implantation sites, live and dead fetuses, early and late resorptions. Fetuses were weighed and sexed externally. Each fetus was examined for the presence of external alterations. Gross necropsy was performed on all organs in all animals.
GLP:	Yes
Year:	1998
Species:	Rat
Strain:	Sprague-Dawley CD
Route of Administration:	Oral gavage
Doses:	0, 100, 500 and 1000 mg/kg/day
Sex:	Female
Exposure Period:	Days 6-19 of gestation

Frequency of Treatment:	Once per day
Control and Treatment Groups:	Yes
Duration of Test:	20 days, days 6 to 20 of gestation
Statistical Methods:	All parameters were statistically analyzed using the TeratoStat System, developed by Statistics Unlimited, Inc., Wellesley, MA. Statistical analyses of maternal body weights, maternal body weight gains, adjusted maternal body weight gains and food consumption were conducted using the Welch Trend Test. The Jonckheere Trend Test was used for Cesarean-section data (Litter Size, Percentages of Live Fetuses, Dead Fetuses, Early Resorptions, Late Resorptions). The Exact Trend Test was used for the Number of Doses with Complete Resorptions. Analysis of Covariance was used for Fetal Weights. The Test on Binomial Proportions was used for Sex Ratios. Fetal external data was analyzed as follows: (1) Litter Incidences of Fetal External Alterations by the One-sided Exact Trend Test and (2) Fetal Incidences of Fetal External Alterations by the One-sided Jonckheere Trend Test.
Results:	The NOEL for fetal toxicity is 100 mg/kg/day, based on significant decreases in fetal body weights at the top two dose levels. The LOEL for fetal toxicity is 500 mg/kg. The NOEL for maternal toxicity is less than 100 mg/kg/day, the lowest dose tested. At the 1000 mg/kg dose level two dams were sacrificed for humane reasons on gestation day 7. Clinical signs noted in all treated dams included oral discharge and abdominalgenital staining. Dams in the top two dose groups (500 and 1000 mg/kg) also displayed abdominal gripping, lacrimation and squinting eyes. Dams at the top dose level (1000 mg/kg) also displayed purple urine, purple abdominogenital staining, decreased locomotion, exophthalmos, splayed hindlimbs and piloerection. Body weights on days 9 and 12 of gestation and body weight gains for the days 6-9 were significantly reduced among all treated groups. Overall body weight gains during treatment were significantly reduced in the top two dose groups and reduced without statistical significance in the low dose group. Adjusted maternal body weight gains were significantly reduced among all treated dams. Food consumption was significantly reduced among all treated groups between days 6-9 and among dams of the two top dose groups on days 9-12. Overall food consumption was significantly reduced for all groups during days 6-20. Significantly decreased fetal body weights were noted among fetuses in the top two dose groups. No significant differences in the incidence of fetal external alterations was noted; one fetus from a single dam receiving 500 mg/kg displayed cleft palate and agnathia. Since these malformations were not dose-related and occurred in a single fetus, they were not considered treatment related. There were no gross necropsy findings. A significant increase in the number of implants among dams in the top two dose groups was not considered treatment-related because implantation occurs prior to treatment.
Data Quality:	Code 2e
References:	Pilot Oral Teratology Study of 7-hydroxybenzofuran technical in Rats, FMC Toxicology Laboratory, FMC Study A98-4958, 1998. Noted in test plan as “Develop. Toxicity”

CRITERIA FOR RELIABILITY CODES

(Adapted from Klimisch et al 1997)

Code of Reliability	Category or reliability
1	**Reliable without restriction**
1a	GLP guideline study (OECD, EC, EPA, FDA, etc.)
1b	Comparable to guideline study
1c	Test procedure in accordance with generally accepted scientific standards and described in sufficient detail
2	**Reliable with restrictions**
2a	Guideline study without detailed documentation
2b	Guideline study with acceptable restrictions
2c	Comparable to guideline study with acceptable restrictions
2d	Test procedure in accordance with national standard methods with acceptable restrictions
2e	Study well documented, meets generally accepted scientific principles, acceptable for assessment
2f	Accepted calculation method
2g	Data from handbook or collection of data
3	**Not reliable**
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system
4	**Not assignable**
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference not yet translated
4e	Documentation insufficient for assessment